

**REMARKS**


With the above amendments, the title of the application as originally identified in corresponding International Application No. PCT/EP01/05557 has been amended to conform with the title as identified in the Declaration which is being concurrently filed in this application.

In addition, claims 4, 6, 8, 9, 15 and 17-20 have been amended to delete multiple dependencies and make those claims singly dependent. A marked-up version of the claims showing the amendments made is annexed for the convenience of the Examiner.

Questions are welcomed by the below-signed attorney for applicant.

Respectfully submitted,

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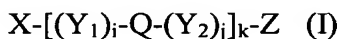
**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Title:**

LINKER SYSTEM FOR ACTIVATING SURFACES FOR BIOCONJUGATION AND  
METHODS FOR THEIR USE

**In the Claims:**

1. Linker system for activating surfaces for bioconjugation having the following general formula (I):



wherein X is a reactive group capable of covalently binding to a surface, Z is a reactive group capable of covalently binding to a biomolecule, with the proviso that X is not Z, Y<sub>1</sub> and Y<sub>2</sub> are independently from each other CR<sub>1</sub>R<sub>2</sub> with R<sub>1</sub> and R<sub>2</sub> being independently from each other H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy, i, j, k are independently from each other an integer in the range from 1 to 10, with the proviso that the total number of C atoms in Y<sub>1</sub> and Y<sub>2</sub>, the C atoms of R<sub>1</sub> and R<sub>2</sub> not included, is in the range of 2 to 100, and Q is a hydrophilic atom or group selected from the group consisting of O, NH, C=O, O-C=O and CR<sub>3</sub>R<sub>4</sub>, wherein R<sub>3</sub> and R<sub>4</sub> are independently from each other selected from the group consisting of H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy and C<sub>1</sub>-C<sub>4</sub> acyloxy, with the proviso that R<sub>3</sub> and R<sub>4</sub> are not H at the same time and that for Q = NH Z is not NH<sub>2</sub>, and wherein in the case of k > 1 the Q's for each [(Y<sub>1</sub>)<sub>i</sub>-Q-(Y<sub>2</sub>)<sub>j</sub>]<sub>k</sub> are independently selected from each other.

2. Linker system according to claim 1 wherein said reactive group X is selected from the group consisting of a disulfide group, a thiol group, a SiW<sub>3</sub> group with W being a hydrolyzable atom or group, and a group capable of forming free radicals such as an

anthrathione group or a derivative thereof, an anthraquinone group or a derivative thereof, a benzophenone group or a derivative thereof.

3. Linker system according to claim 2 wherein said hydrolyzable atom or group W is selected from the group consisting of halides, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> acyloxy and amino groups.

4. (Amended) Linker system according to ~~any of the preceding claims~~ claim 1, wherein said reactive group Z is capable of nucleophilic substitution reactions, nucleophilic addition reactions, Diels-Alder reactions or radical substitutions.

5. Linker system according to claim 4 wherein said reactive group Z is selected from the group consisting of a reactive double bond, a diene group, a dienophilic group, an epoxy group, an aldehyde group, a hydroxyl group, a carboxylic acid group, an active ester group, an amino group, a disulfide group, a thiol group, an aziridine group, an isocyanate group, an isothiocyanate group, an azide group and a reactive leaving group.

6. (Amended) Surface carrying a linker system according to ~~any of claims 1 to 5~~ claim 1.

7. Surface according to claim 6 wherein said linker system forms a patterned array.

8. (Amended) Surface according to claims 6 ~~or 7~~, wherein said surface is selected from the group consisting of a SiO<sub>2</sub> surface of a silicon wafer, glass, quartz, fused silica, gold and a polymer.

9. (Amended) Surface according to any of claims 6 ~~to 8~~, wherein said linker system is covalently bonded to a biomolecule.

10. Surface according to claim 9 wherein said biomolecule is a partner of a specifically interacting system of complementary binding partners.

11. Surface according to claim 10 wherein said specifically interacting system of complementary binding partners is based on nucleic acid/complementary nucleic acid, peptide nucleic acid/nucleic acid, enzyme/substrate, receptor/effector, lectin/sugar, antibody/antigen, avidin/biotin or streptavidin/biotin interaction.
12. Surface according to claim 11 wherein said nucleic acid is a DNA or RNA.
13. Surface according to claim 12 wherein said DNA or RNA is an oligonucleotide or an aptamer.
14. Surface according to claim 11 wherein said antibody is a polyclonal, monoclonal, chimeric or single-chain antibody or a functional fragment or derivative of such antibodies.
15. (Amended) Process for the detection of a biomolecule which is a partner of a specifically interacting system of complementary binding partners comprising the steps of
- a) contacting a surface according to ~~any of claims 10 to 14~~ claim 10 with a sample suspected to contain the complementary binding partner,
  - b) removing non-specifically bound sample components in a washing step, and
  - c) detecting the specifically bound sample components.
16. Process according to claim 15 wherein for said detecting a colored, fluorescent, bioluminescent, chemoluminescent, phosphorescent or radioactive label, an enzyme, an antibody or a functional fragment or derivative thereof, a protein A/gold based system, a biotin/avidin/streptavidin based system or an enzyme electrode based system is used.
17. (Amended) Process for the isolation of a biomolecule which is a partner of a specifically interacting system of complementary binding partners comprising the steps of
- a) contacting a surface according to ~~any of claims 10 to 14~~ claim 10 with a sample suspected to contain the complementary binding partner,

- b) removing non-specifically bound sample components in a washing step, and, optionally,
- c) eluting the specifically bound sample components.

18. (Amended) Use of a surface according to ~~any of claims 10 to 14~~ claim 10 as an affinity matrix.

19. (Amended) Use of a surface according to ~~any of claims 10 to 14~~ claim 10 in a sensor chip or biochip.

20. (Amended) Medical or diagnostic instrument comprising a surface according to ~~any of claims 10 to 14~~ claim 10.